EARLY ONSET OF MENSTRUATION IN A 45,X GIRL

Ichiro MURANO, Kiyosato MATSUO, and Tadashi KAJII

*Department of Pediatrics, Yamaguchi University School of Medicine,
Ube, Yamaguchi 755, Japan*

Summary A girl with short stature developed breasts at age 10 and began menarche at 10.3 years. When examined by us at age 15 years, she had had regular menstrual cycles. Chromosome analyses using PHA- and EB virus-stimulated lymphocytes and cultured skin fibroblasts from both elbows all revealed an exclusively 45,X karyotype. Both buccal smears and hair root cells were negative for the X-chromatin.

INTRODUCTION

Patients with non-mosaic Turner syndrome usually suffer from the absence of breast development and primary amenorrhea. The degree of estrogen secretion in as many as 5 to 10% of the patients, however, is sufficient to initiate breast development at puberty. In a small percentage of this group, the level of secretion is sufficient to initiate menses, and a very small number of them maintain normal ovarian function. To our knowledge, 21 patients with a non-mosaic 45,X karyotype in the literature had spontaneous menstrual cycles for at least a year (*cf.* Kohn *et al.*, 1980 and Wray *et al.*, 1981 for references). Their ages at menarche ranged from 10.5 to 17 years. We wish to report a 45,X girl whose onset of menstrual cycles was 10.3 years, the youngest known.

CASE REPORT

This 15-year-old girl was the product of a normal pregnancy, with a birth weight of 2,700 g and has been noticeably short most of her life. Initial breast development occurred at age 10 years, menarche began at age 10.3 years and her menstrual cycles thereafter followed a regular 4 weeks interval schedule. She visited our clinic for evaluation of her short stature at age 14 years. At this time, our examination revealed her height as 130.5 cm (-4.28 SD) and her weight as 39.9 kg (-1.25 SD) (Fig. 1). She was hirsute, especially in the forearms, and has a low occipital

Received September 1, 1984; revised version received February 5, 1985

Fig. 1. The patient at 15 years.

hairline, a short, webbed neck, abundant, curly hair, cubitus valgus, and short fifth fingers. Her ears were normal as were her palate and her finger- and toe-nails. Her breasts were at Tanner stage III, her pubic hair was Tanner stage IV, and she had dense axillary hair. Her dermatoglyphic patterns were normal, except for the presence of the hypothenar loop patterns. Her total finger ridge count was 143.

The serum estradiol level at the follicular stage was 140 pg/ml (normal range; 34–223 pg/ml). Basal serum gonadotropins were high at LH 62 mIU/ml, FSH 19 mIU/ml, and their response to LH-RH (100 μ g/m² given i.v. in one bolus) was exaggerated, as compared to control pubertal females (Fig. 2). Her carpal bone age at 14 years was estimated as that of a 16 year old. CT scan of the brain, electrocardiography, and intravenous pyelography yielded no indications of abnormalities.

Her basal body temperature assessed through three consecutive cycle registered diphasic patterns, an indirect evidence of ovulation.

Cytogenetic studies. Chromosome analyses on PHA- and EB virus-stimulated PB lymphocytes and fibroblast cultures from the skin of the left and right elbows all revealed a 45,X karyotype (Table 1). There was no metaphase with a 46,XX karyotype. Buccal smears from both cheeks and hair-root preparations from both sides of the head were found to be X-chromatin negative (Table 2).

Fig. 2. Baseline LH and FSH levels and their response to $100 \mu\text{g}/\text{m}^2$ o/v/LH-RH are shown. Although baseline levels of the gonadotropins were elevated, their responses to LH-RH were markedly exaggerated. Normal ranges are from the study by Aono *et al.* (1973).

Table 1. Chromosome analysis.

Tissue	Chromosome counts				Modal karyotype
	44	45	46	Total	
PB lymphocytes					
PHA-stimulated	8 ^a	81 (4)	0	89 (4)	45,X
EB virus-stimulated	4 ^a	69 (3)	0	73 (3)	45,X
Skin fibroblasts					
Left elbow	21 ^a	249 (2)	2 (2) ^b	272 (4)	45,X
Right elbow	20 ^a	199 (2)	1 (1) ^c	220 (3)	45,X
Total	53	598 (11)	3 (3)	654 (14)	

(), No. cells G-banding karyotyped. ^a Random loss. ^b Dp⁻, +small metacentric; +E.
^c +acentric.

DISCUSSION

As mentioned earlier, we are aware of 22 patients, including the patient we described, with an apparently non-mosaic 45,X karyotype, who spontaneously menstruated for at least a year (Table 3). The presence of a mosaic 46,XX cell line

Table 2. X-chromatin test.

Tissue	No. cells counted	No. cells with X-chromatin-like body
Buccal smear		
Left buccal mucosa	500	0
Right buccal mucosa	500	1
Hair root		
Left temporal	771	1
Right temporal	853	0
Total	2,624	2

cannot be totally ruled out in these patients, especially in the five patients in whom only PB lymphocytes were karyotyped. Of the 22 women, 11 of them had become pregnant one time or more, resulting in 14 pregnancies. Eight normal infants, a 21 trisomic infant, two stillbirths, and three spontaneous abortions were the outcomes of these 14 pregnancies. Thus, reproductive failure is frequent and the risk of bearing an abnormal offspring is considerable among the 45,X women who conceive.

The age range at which menarche occurred in these 45,X women was normal, from 10.5 to 17 years. The age at which menarche begun in our patient, 10.3 years, is the youngest known. Many 45,X women who menstruate appear to lose their ovarian function before 30 years of age. Thus, the reproductive life span in these women is markedly shorter than that in normal women.

It is known that germ cells are present in 45,X human embryos (Singh and Carr, 1967), but their attrition is greatly increased compared with those in 46,XX embryos (Weiss, 1971). Thus, in the majority of 45,X girls, the gonads are totally or largely depleted of primordial follicles by the time of puberty. In a few of the patients with 45,X, this process may progress more slowly than that of typical Turner syndrome patients, however. These women are assumed to have a few surviving germ cells which are sufficient to initiate menses at puberty. They are likely to display early biological aging because of a small number of surviving germ cells in their ovaries. This observation helps explain the high frequency of abnormalities among the conceptuses of the 45,X women.

Table 3. 45,X women with menstruation.

No.	Reference ^a	Karyotyping			X-chromatin test			Age (yr) at		Outcome of pregnancy
		PB lymphocytes	Skin fibroblasts	Ovary	Other tissues	Buccal smear	Neutrophils	Other tissues	Menarche	Menopause
1	Bahner <i>et al.</i> , '60		+		+ ^b	+	+		17	>39
2	Nakashima <i>et al.</i> , '71	+	+			+			16	21
3	Grace <i>et al.</i> , '73	+				+			13	21
4	Groll & Cooper, '76	+				+			13	>29
5	Philip & Sele, '76	+	+	+	+ ^c	+			— ^j	
6	Lajborek-Czyz, '76	+				+			14	>22
7	Shokeir, '78	+	+			+			13	20
8	"	+	+			+			14	17
9	King <i>et al.</i> , '78	+	+	+	+ ^c				17	>21
10	Kohn <i>et al.</i> , '80	+	+			+			19	>31
11	Wray <i>et al.</i> , '81	+	+	+	+ ^d	+			15	>35
12	Monardo, '65	+				+			11	28
13	Zarate <i>et al.</i> , '69	+				+			14	19
14	Weiss, '71	+				+	+	+ ^g	11	>14
15	Hausmann & Goebel, '72	+	+			+	+		14	>20
16	Calverly & Buler, '73	+	+			+		+ ^h	12	20
17	Friedrich <i>et al.</i> , '74	+	+	+		+			10	24
18	Gilboa & Rosenberg, '75	+	+	+		+			13	14, 5
19	Kemmann <i>et al.</i> , '77	+	+	+	+ ^c				12	>16
20	Lisker <i>et al.</i> , '79	+	+	+	+ ^b	+			12	18
21	Lock <i>et al.</i> , '79	+	+		+ ^e				15	>18
22	Present case	+	+		+ ^f	+		+ ⁱ	10	>15

^a Cf. Wray *et al.*, '81 for references Nos. 1-10; cf. Kohn *et al.*, '80 for references 12-21. ^b Bone marrow. ^c Uterus. ^d Fascia. ^e Uterine adnexa. ^f EB virus-stimulated lymphocytes. ^g Smooth muscle. ^h Skin fibroblasts. ⁱ Hair root. ^j Menses on cyclic estrogen.

REFERENCES

- Aono, T., Minagawa, J., Kinugasa, T., Tanizawa, O., and Kurachi, K. 1973. Response of pituitary LH and FSH to synthetic LH-releasing hormone in normal subjects and patients with Sheehan's syndrome. *Am. J. Obstet. Gynecol.* **117**: 1046-1052.
- Kohn, G., Yarkoni, S., and Cohen, M.M. 1980. Two conceptions in a 45,X woman. *Am. J. Med. Genet.* **5**: 339-343.
- Singh, R.P., and Carr, D.H. 1966. The anatomy and history of XO human embryos and fetuses. *Anat. Rec.* **155**: 369-375.
- Weiss, L. 1971. Additional evidence of gradual loss of germ cell in the pathogenesis of streak ovaries in Turner's syndrome. *J. Med. Genet.* **8**: 540-544.
- Wray, H.L., Freeman, M.V.R., and Ming, P.L. 1981. Pregnancy in the Turner syndrome with only 45,X chromosomal constitution. *Fertil. Steril.* **35**: 509-514.